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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/008,945	01/20/98	GRIFFITH L	20220-0169

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1651	31

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/068945	Griffith et al
Examiner	**Group Art Unit**
Naff	1657

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 2/05/01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 25-52 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☒ Claim(s) 25-52 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received:_____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s)._____ ☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892 ☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948 ☐ Other_____

Office Action Summary

The request filed on 2/15/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/008,945 is acceptable and a CPA has been established. An action on the CPA follows.

The name of the first inventor has been changed to Linda G. Griffith as requested in the petition under 35 C.F.R. 1.182 of 3/6/01.

The preliminary of 3/6/01 and the supplemental amendment of 3/23/01 have been. The preliminary amendment canceled claims 1-9, 11, 12 and 14-24, and added claims 25-43. The supplemental amendment added claims 44-52.

Claims examined on the merits are 25-52 which are all claims in the application.

The text of those sections of Title 35; U.S. Code not included in this action can be found in a prior Office action.

Claims 44-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Adequate support is not found in the specification for completing hardening after introduction of the composition into an animal as now claimed. Previous claim 1 encompassing completing hardening after introduction is not adequate support. There must be disclosure of completing hardening as claimed rather than merely a disclosure of such breadth as to encompass what is claimed.

Claims 25, 26, 28-35 and 37-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point

out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25, 26, 28-35 and 37-43 confusing and unclear by "anatomic shape" in claims 25 and 35 being uncertain as to meaning and scope. It is uncertain as to shapes that are anatomic and not anatomic.

Claims 44-52 are confusing and unclear by claim 44 being unclear as to the meaning and scope of "completing" hardening after introduction of the composition into an animal, and not having antecedent basis for completing hardening. Does this mean that there is partial hardening before introduction or is something else intended such as all hardening is completed after introduction? If there is partial hardening before introduction, then this should be required in the claim provided there is support in the specification. If partial hardening is not carried out before introduction, then applicants should explain what is meant by completing hardening after introduction.

In claim 46, the meaning and scope of "hardening is initiated before the step of introducing" is uncertain. Does this mean that components have been mixed that can subsequently harden or does it mean that some hardening has occurred before introduction of the composition into an animal?

Claims 27-33, 36-42 and 44-51 are rejected under 35 U.S.C. 102(a) as being anticipated by Atala et al (abstract presented at the annual meeting of American Academy of Pediatrics on Oct. 10-15, 1992).

The claims are drawn to a method of introducing cells into an animal by forming a cell-polymeric composition containing cells and a polymer, introducing the composition into an animal and hardening the polymer to

form a hydrogel. Also claimed is an implant that is the cell-polymeric composition suitable for implantation into an animal before hardening.

Atala et al disclose mixing a suspension of chondrocytes with alginate, and injecting the resultant chondrocyte/alginate solution with a needle subcutaneously into a mouse where the alginate is gelled and cartilage is formed. The method of Atala et al and the chondrocyte/alginate solution used therein are encompassed by the present claims. Mixing a cell suspension with the alginate as disclosed by Atala et al will inherently initiate hardening before introduction as in claim 46.

Stating that Alan B. Retik (who is an author) is not an inventor in a 37 C.F.R. 1.132 Declaration does not remove Atala et al as a reference. The present application contains Keith T. Paige as an inventor who is not an author. Even with Retik not being an inventor, the inventive entity of the present invention is different from the authorship of the abstract.

Claims 27-33, 36-42 and 44-51 are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The Atala et al abstract applied above does not contain Paige as an author whereas Paige is a co-inventor of the claimed invention along with co-inventors Griffith-Cima, Vacanti and Atala who are co-authors of the abstract. Since the abstract discloses a method and implant within the scope of the present claims, the claims encompass subject matter which the present inventive entity did not invent. It is not seen how Paige can be a co-inventor of the method and implant of the abstract

along with co-inventors who are co-authors of the abstract, and not be a co-author of the abstract.

Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Atala et al in view of Nevo et al (4,642,120).

The claim requires the cells to be osteoblasts.

Atala et al is described above.

Nevo et al disclose (col 1, lines 5-10 and col 3, lines 62-68) repairing cartilage or bone by implanting a gel containing chondrocytes or bone marrow stem cells .

It would have been obvious to substitute osteoblasts for the chondrocytes of Atala et al when desiring to repair bone as suggested by Nevo et al since these are known bone forming cells.

Claims 25, 26, 28-35 and 37-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atala et al (abstract) in view of Nevo et al (4,642,120) and Vacanti et al (5,041,138), and if necessary in further view of Vacanti et al (J. Ped. Surg.).

Claim 25 requires the cell-polymeric composition to be hardened before introduction into an animal, claim 35 requires an implant containing the cell-polymeric composition hardened into a desired anatomical shape, and claims 34 and 43 require the cells to be osteoblasts.

Atala et al and Nevo et al are described above.

Vacanti et al ('138) disclose forming a molded matrix containing chondrocytes for implanting to form cartilage (col 3, lines 17-43).

Vacanti et al (J. Ped. Surg.) disclose forming a polymer-cell scaffold for implanting wherein a desired shape of the polymer scaffold

may be obtained by solvent casting or compression molding (page 3, right col).

It would have been obvious to gel the chondrocyte-containing alginate solution of Atala et al to provide a desired body part shape, and then implant the shaped gel as suggested by Nevo et al implanting a gel containing cells to repair a defect and Vacanti et al ('138), and if needed Vacanti et al (J. Ped. Surg.), disclosing implanting molded scaffolds containing cells. When desiring to repair bone as suggested by Nevo et al, the use of osteoblasts as the cells would have been obvious since these are known bone forming cells.

The comments set forth above in regard to the declaration also apply to this rejection.

The amendments of 3/6/01 and 3/23/01 do not respond to rejections over Atala et al.

Claims 25, 26, 28-35 and 37-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Schlameus et al (5,294,446).

Schlameus et al disclose mixing osteoprogenitor cells with a solution of alginate, gelling the alginate to form microcapsules containing the cells and implanting the microcapsules to regenerate bone (col 3, lines 51-68, and col 4, lines 30-40).

The present claims encompass mixing cells with an alginate solution to form a cell-alginate composition, and gelling the alginate to form microcapsules as disclosed by Schlameus et al.

Applicants urge that Schlameus et al does not disclose implanting a hydrogel having an anatomic shape as claimed. However, the capsules of Schlameus et al can be considered to be an anatomic shape.

Claims 27-33, 36-43 and 44-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schlameus et al in view of Barry et al (5,266,326) and Dionne et al (WO 92/19195), and if necessary in further view of Bhatnagar (5,354,736).

The claims requires hardening the cell-polymeric composition after introduction into an animal.

Schlameus et al is described above.

Berry et al disclose (abstract and col 3, lines 40-45) injecting an alginate solution and a calcium chloride solution into intra-articular space following closure of a surgical site, and allowing the alginate to gel *in situ* to prevent intra-articular adhesions. The alginate solution may contain drugs and other therapeutic agents (col 6, lines 52-55).

Dionne et al disclose (page 4, lines 5-16) forming an implantable vehicle containing cells by immobilizing cells in a hydrogel matrix core and surrounding the core with a jacket or membrane that is permselective and prevents the cells in the core from immunological attack. The core and membrane can be made of the same composition hydrogel (page 9, lines 21-22) and can be alginate cross-linked with calcium ions (page 9, lines 3-6, and page 18, line 10). It is possible for a single, continuous hydrogel matrix to provide both immunoisolation and support or immobilization (page 53, lines 5-24). It is further disclosed (page 18, lines 18-24) that a hydrogel matrix precursor solution can be included but not exposed to polymerizing conditions. In the case of sodium alginate, a hydrogel will form after implantation as calcium ions are scavenged from surrounding tissues.

Bhatnagar discloses (abstract and col 13, lines 45-49) carrying out soft and hard tissue repair by implanting a hydrogel matrix that promotes cell attachment to the matrix and cell migration into the matrix. The hydrogel matrix results in a three dimensional environment that causes cells to differentiate (col 13, lines 50-55). When soft tissue repair is carried out, injection can be prior to gelation and the gel formed in situ (col 13, lines 58-60).

It would have been obvious to omit forming microcapsules and inject the cell-containing alginate solution of Schlameus et al into intra-articular space as suggested by Berry et al to allow *in situ* gel formation to prevent intra-articular adhesions, and as suggested by Dionne et al disclosing forming an alginate hydrogel containing cells after implantation as calcium ions are scavenged from surrounding tissues as an alternative to forming an alginate gel matrix containing cells and implanting the matrix. If needed, further suggestion is provided by Bhatnagar disclosing forming a hydrogel *in situ* for tissue repair. The disclosure by Berry et al that drugs or other therapeutic agents can be in the injected alginate solution would have suggested that the cells of Schlameus et al can be present in the alginate solution when injected to obtain the tissue repair function of the cells in addition to preventing adhesions as disclosed by Berry et al.

Contrary to applicants argument, the secondary references clearly suggest injecting a composition that is hardened after injecting. Differences of the secondary references from the invention that the claims do not exclude do not lead away from not following the teachings of the references in regard to hardening after introduction. As to

anatomic shape, the gel of each reference can be considered to be an anatomic shape depending on ones definition of this term.

Claims 25, 26, 28-35 and 37-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schlameus et al in view of Nevo et al (4,642,120) and Vacanti et al (5,041,138), and if necessary in further view of Vacanti et al (J. Ped. Surg.) for reasons in the previous office action as repeated below.

Claims 25 and 35 require hardening the cell-polymeric composition into a desired anatomical shape.

The references are described above.

It would have been obvious to form the alginate gel of Schlameus et al into a molded anatomical shape instead of microcapsules as suggested by Nevo et al implanting a gel containing cells that is not in the form of microcapsules and by Vacanti et al ('138), and if needed Vacanti et al (J. Ped. Surg.), disclosing implanting molded scaffolds containing cells. Nevo et al and Vacanti et al ('138) use chondrocytes as the cells implanted, and it would have been obvious to implant these cells for their known cartilage forming function.

Contrary to applicants' arguments, the formation of an anatomic shape is obvious in view of Vacanti et al forming a molded shape. The fact that Vacanti et al may use fibers to form a scaffold does not lead away from molding to a desired body part shape since it would have been expected that a hydrogel can also be molded to have a desired body part shape.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone

number is (703) 308-0520. The examiner can normally be reached on Monday-Thursday and every other Friday from about 8:30 AM to about 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, a message can be left on voice mail.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn, can be reached at telephone number (703) 308-4743.

The fax phone number is (703) 305-3014 or 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 1651

DMN
7/30/01